REMARKS

The Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. Amendments

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

Claims 45 and 60 are currently amended to advance prosecution of the application. In particular, claims 45 and 60 have been amended to incorporate the limitation in claims 47 and 61, respectively, which are requested to be cancelled. As amended, claims 45 and 60 recite "and greater than about 70% of total amino acids of the transmembrane domain are members of the group consisting of F, I, W, Y, L, V, M, P, C, and A." These amendments do not add new matter and entry thereof is respectfully requested.

After amending the claims as set forth above, claims 42-45, 49-55, 58-60, and 62-66 are now pending in this application.

II. Claim Rejections – 35 U.S.C. § 103

Claims 42-44, 49-53, 55 and 58-66 are rejected under 35 U.S.C. § 103 as being unpatentable over Swartz and MacKinnon in view of Carrère-Kremer *et al.*, Rokitskaya *et al.*, and Smith JP. The Office Action states that Swartz and MacKinnon "disclose a method of measuring the changes in membrane permeability induced by ion channel activity in the presence and absence of test compounds." The Office Action further states that Swartz and MacKinnon does not disclose using HCV p7. However, the Office Action indicates that it would be obvious to use HCV p7 as taught by Carrère-Kremer *et al.* in the methods of Swartz and MacKinnon. The Applicants respectfully traverse the rejection because none of the cited references disclose that HCV p7 is an ion channel protein.

The Applicants believe that they were the first to demonstrate that HCV p7 is an ion channel protein. *See* Davor Pavlović, David C. A. Neville, Olivier Argaud, Baruch Blumberg, Raymond A. Dwek, Wolfgang B. Fischer, and Nicole Zitzmann, "*The hepatitis C virus p7 protein forms an ion channel that is inhibited by long-alkyl-chain iminosugar derivatives*," PNAS 100(10):6104-6106 (2003). Therefore, prior to the Applicants' work, any indication that HCV p7 might be an ion channel protein was merely speculative, and there would not have been a reasonable expectation of success that a useful screening method could be provided by utilizing HCV p7.

Contrary to the assertion in the Office Action, Carrère-Kremer *et al.* does not disclose that HCV p7 is an ion channel protein. In particular, the Office Action asserts that Carrère-Kremer *et al.* disclose that "the transmembrane domains induce leak when associated with ER membranes (page 3728, paragraph 2 of col. 1)." This is factually incorrect. At the cited section, Carrère-Kremer *et al.* state:

> As shown by immunofluorescence studies and the endo H sensitivity of CD4-p7, a large fraction of p7 is retained in an early compartment of the secretory pathway, which is likely the ER, suggesting that an ER retention signal is present in p7. The transmembrane domains of HCV envelope glycoproteins are signals for ER retention (for a review, see reference 39), and a similar localization signal might be contained in p7. However, the difference between the transmembrane domains of HCV envelope proteins and p7 is that ***the ER retention signal contained in p7 is leaky***.

Therefore, Carrère-Kremer *et al.* does not state that HCV p7 makes the ER "leaky." Rather, Carrère-Kremer *et al.* characterize the putative ER retention signal as "leaky." By characterizing the putative ER retention signal as "leaky," Carrère-Kremer *et al.* indicate that the ER retention signal does not effect 100% retention of HCV p7 in the ER and as such, HCV p7 may be present elsewhere in the cell. The Applicants respectfully request that this portion of Carrère-Kremer *et al.* be reviewed again and the rejection under 35 U.S.C. § 103 be reconsidered.

The Office Action also indicates that "Carrère-Kremer *et al.* suggest that HCV p7 may be able to modify membrane permeability (page 3729, paragraph 2 of col. 2)." However, at the cited section, Carrère-Kremer *et al.* indicate that any suggestion that HCV p7 is a channel protein is ***merely speculative***, stating:

> The recognition of virus proteins capable of enhancing membrane permeability has led to the description of a new family of virus proteins, called viroporins (3). Structurally, viroporins are generally short proteins containing about 50 to 120 amino acid residues. They are integral membrane proteins with at least one membrane-spanning domain and tend to form oligomers. Based on the structural features of HCV p7, it is tempting to include this protein in the viroporin family, as suggested for pestivirus p7 (21). However, ***experimental data will be needed to demonstrate whether, like the members of this family, HCV p7 is able to modify membrane permeability***.

In particular, Carrère-Kremer *et al.* state that "experimental data will be needed to demonstrate whether...HCV p7 is able to modify membrane permeability." As indicated above, the Applicants believe that they were the first to provide "experimental data" that "HCV p7 is able to modify membrane permeability." Based on statements by Carrère-Kremer *et al.*, any suggestion that HCV p7 is able to modify membrane permeability was merely speculative prior to the Applicants' own work. Therefore, based on statements by Carrère-Kremer *et al.*, a method of screening for an inhibitor of HCV p7 protein by observing a decrease in permeability in a HCV p7-containing membrane would have been merely speculative and not obvious.

For these reasons, reconsideration and withdrawal of the rejections under 35 U.S.C. § 103, over Swartz and MacKinnon in view of Carrère-Kremer *et al.*, Rokitskaya *et al.*, and Smith JP are respectfully requested.

III. Claim Rejections – 35 U.S.C. § 112, second paragraph

Claims 45, 47, 60 and 61 stand rejected under 35 U.S.C. § 112, second paragraph, allegedly as being indefinite for failing to recite a limitation that is further limiting. The Applicants respectfully disagree with the rejection. However, in order to further prosecution, claims 47 and 61 have been cancelled and claims 45 and 60 have been amended to incorporate the limitations of cancelled claims 47 and 61, respectfully. As amended, claims 45 and 60 recite limitations that are further limiting.

For these reasons, reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, second paragraph, for indefiniteness are requested.

IV. Conclusion

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

If any extensions of time are needed for timely acceptance of papers submitted herewith, the Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorize payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date December 14, 2006 By

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